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Right atrial extension of Wilms' tumor

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Summary

Background: Right atrial involvement in children with Wilms' tumor (nephroblastoma) is a very rare phenomenon.

Case report: The authors present four children with nephroblastoma, in whom the tumor involved the inferior vena cava and the right atrium. In two children the intracardiac tumor extension was asymptomatic, while the other two had Budd-Chiari syndrome. Therapeutic management included initial three-drug chemotherapy in three patients, and primary tumor excision in one child, since the venous involvement had been not diagnosed. In each child, the therapeutic strategy was individualized and tailored to the course of the disease. Two patients were cured. The child with bilateral Wilms' tumor died due to disease progression. Another child died suddenly at home in the course of an intermission between consecutive cycles of successful chemotherapy.

Conclusions: The extension of Wilms' tumor to the great vessels and the right atrium indirectly affects the final outcome. Preoperative chemotherapy in children with Wilms' tumor invading the inferior vena cava and the right atrium is the method of choice. The extent of surgery depends on the preliminary chemotherapy results.

key words: **Wilms' tumor • cardiac involvement • children**

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BACKGROUND

Wilms' tumor (nephroblastoma) is the most common renal malignancy in childhood. It is characterized by a strong tendency to invade blood vessels, especially within the tumor itself. Direct extension of the tumor mass through renal veins into the inferior vena cava is noted in 4–10% of patients [1,2]. Much more rarely does the mass extend as far as the right atrium, and in such cases marked diagnostic and therapeutic problems arise due to the diversified dynamics of the disease development and individualized therapeutic management.

These considerations warrant a description of four children with Wilms' tumors extending through the inferior vena cava into the right atrium, as well as a comparison of the authors' experience with observations presented by other investigators.

The authors performed a retrospective analysis of 196 children treated for Wilms' tumor in the years 1979 through 1999. Only four of them showed massive tumor invasion through the inferior vena cava into the right atrium. The diagnosis was established, and the treatment of the hepatic vein and right atrium lesions was monitored by complex echocardiographic methods (2-DE), including Doppler and color echocardiography (2-DD). The description of the cases is arranged according to the chronological order in which the patients were diagnosed.

CASE STUDIES

Patient no. 1

A 4-year old girl presented with a 3-week history of abdominal pain. Clinical examination revealed a large mass occupying the right side of the abdomen. Abdominal ultrasound and intravenous urography demonstrated a tumor in the right kidney, and the child was referred for surgery. The intraoperative findings disclosed a tumor measuring 22 cm × 18 cm × 16 cm with an infiltrated capsule. The renal vein and the inferior vena cava showed a flask-like distension and were filled with tumor thrombi. The renal pedicle was ligated and severed, and a right nephrectomy and tumor excision was performed, while the tumor mass was left inside the veins. Immediately after surgery, echocardiography showed the presence of ac tumor mass obstructing the hepatic segment of the inferior vena cava and the hepatic veins and extending up to the right atrium. There, the mass formed a solid tumor arising from a wide pedicle, measuring 1.5 cm × 1.2 cm, which was situated at the opening of the inferior vena cava and did not obstruct blood flow from the superior vena cava. The patient received chemotherapy, consisting of dactinomycin, vincristine, epirubicin and cyclophosphamide (National Wilms' Tumor Study – NWTS), and the tumor bed was irradiated. The histopathological results pointed to a favorable tumor type, and numerous clusters of tumor cells inside blood vessels. Follow-up echocardiography demonstrated gradual reduction of the intracaval and atrial tumor mass. At present, 16 years after the completion of treatment, abdominal echo and ultrasound show the patient to be free of any abnormalities within the inferior vena cava, hepatic veins and right atrium.

Patient no. 2

A 3-year old girl was admitted for abdominal pain, vomiting, dehydration and oliguria. She presented with a palpable mass, distending the left side of the abdomen, and ascites. Urography showed no excretory function in the left kidney; chest x-ray films were normal. A Wilms' tumor with a favorable histology was confirmed by thin-needle biopsy. Subsequently, the patient was started on chemotherapy, consisting in dactinomycin (15 ucg/kg of body mass) administered over 5 days with vincristine added on days 1 and 8. On the tenth day of therapy the patient suddenly deteriorated, presenting with loss of consciousness, symptoms of pulmonary edema, and two episodes of left-sided seizures. Echocardiography showed the a tumor thrombus obstructing the hepatic segment of the inferior vena cava, partially obstructed hepatic veins, and a uniform tumor with a wide pedicle that filled approximately one-third of the right atrium and protruded into the right ventricle via the tricuspid valve at each diastole (Fig. 1). The child was referred for radiation therapy and received a total dose of 1500 cGy to the tumor site over 10 days. This resulted in tumor shrinkage both within the kidney and the heart, the resolution of ascites, and general clinical improvement. A left nephrectomy was performed along with tumor excision, while the pathological masses were left in situ within the large vessels. The histological results showed a tumor with favorable structure and multiple necrotic foci. Chemotherapy was continued, using dactinomycin, vincristine and epirubicin according to the NWTS-DD protocol. A follow-up echocardiogram showed shrinkage of the tumor situated in the right atrium. Eight months into therapy the child, who had been doing very well and was staying at home, suddenly died.

Patient no. 3

A 4-year old girl with a 3-week history of severe abdominal pain was hospitalized due to suspicion of appendici-

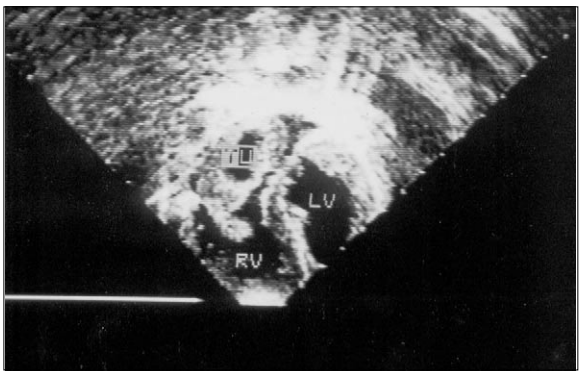

Figure 1. Transthoracic ECHO (four-chamber view). Opacification of the right atrial chamber by tumor masses and protrusion into the right ventricular inflow during diastole. LV – left ventricle. RV – right ventricle. TU – tumor mass.

tis. The abdominal ultrasonography and intravenous pyelography showed a large mass in the right kidney and a lesion on the left side, involving the lower pole and central part of the kidney. Chemotherapy was started according to the SIOP-9 protocol (Societe Internationale de Oncologie Pediatrique), with dactinomycin, vincristine and epirubicin; the tumor masses decreased, but were still inoperable. Continued chemotherapy maintained the disease at the same stage, until ascites suddenly developed. The follow-up cardiac ultrasound and echo showed the tumor mass extending from the right kidney into the inferior vena cava and right atrium. Radiation therapy was initiated, and the child received 1000 cGy to the tumor site. The original chemotherapy protocol was replaced by carboplatin, VP-16, and isophosphamide. The intensified therapy did not result in improvement, and the disease progressed both within the abdominal cavity and in the right atrium, leading to the death of the patient.

Patient no. 4

A 3-year old boy underwent an appendectomy due to acute abdominal symptoms. The appendix showed inflammatory lesions, and a large volume of transudative fluid was found in the peritoneal cavity. The postoperative course was uneventful. Three weeks later the child suddenly deteriorated, presenting with rapidly increasing ascites, edema of the scrotum, lower limbs, neck and eyelids. On admission the patient presented in apparent distress and with dyspnea. Physical examination revealed depressed right vesicular murmur and hepatomegaly (the liver palpable 4 cm below the right costal arch). His blood pressure was 100/65 mmHg, with periodic elevation up to 160/90 mmHg, while the pulse was 100 beats/min. Laboratory data revealed a WBC of $18.7 \times 10^3/\mu L$, a platelet count of 568×10^3, total protein of 56 g/l, AspAt 168 U/l (normal range: 15–59 U/L), AlAt 108 U/L (normal range: 7–8 U/l), prothrombin index 60%, fibrinogen 1.5 g/l, D-dimers 1.0 mg/l. Abdominal ultrasonography confirmed a large volume of fluid in the peritoneal cavity and a grossly distended inferior vena cava, which was filled with a mass showing the density of soft tissue, extending as far as the right atrium. The mass also filled both renal veins, especially on the right side, and the hepatic veins. The right kidney was slightly enlarged, with a central hyperechogenic mass modeling the superior and central calyces Computer tomography showed a tumor mass $5 \times 3 \times 3$ cm in size, enhanced after contrast injection to 80 H.U. (Fig. 2). Echography revealed the presence of fluid in the pericardium, right pleura and peritoneal cavity, as well as a large tumor, which almost completely filled the right atrium. There was continuity between the tumor and the thrombus contained within the inferior vena cava, and blood flow from the superior vena cava to the tricuspid valve was partially obstructed. The ostium of the right hepatic vein was blocked with tumor masses extending from the inferior vena cava, and the distended left hepatic vein showed a considerable narrowing, through which it drained into the right atrium. The distended right azygos vein served as a conduit for blood flowing from the lower part of the body to the distended superior vena cava. The clinical presentation combined with the findings obtained in additional studies suggested the diagnosis of Wilms' tumor involving the right kidney and extending into the vena cava and the right atrium. Chemotherapy was instituted according to the SIOP protocol (dactinomycin, vincristine, epirubicin continued over 6 weeks). Initially, the patient required intensive care, blood pressure monitoring, oxygen therapy and forced diuresis. After 1 week of therapy, ascites and upper extremity edema resolved; the patient was no longer bed-ridden and started to play. After 6 weeks of treatment the size of the tumor mass in the right kidney was reduced by half, though the hepatic segment of the inferior vena cava was still obstructed by tumor thrombi. Patency was restored in its distal segment and the ostium of the hepatic veins, however, and the right atrium tumor had shrunk markedly, involving only the area adjacent to the ostium of the inferior vena cava and no long obstructing flow within the atrium. The patient was referred for surgical treatment. Using a transperitoneal approach, the macroscopically normal right kidney was excised and a whitish mass, which quite closely adhered to the vascular walls, was removed from the left renal vein and inferior vena cava by a venotomy. Transesophageal echography visualized fixed pathological masses in the right atrium, which caused no hemody-

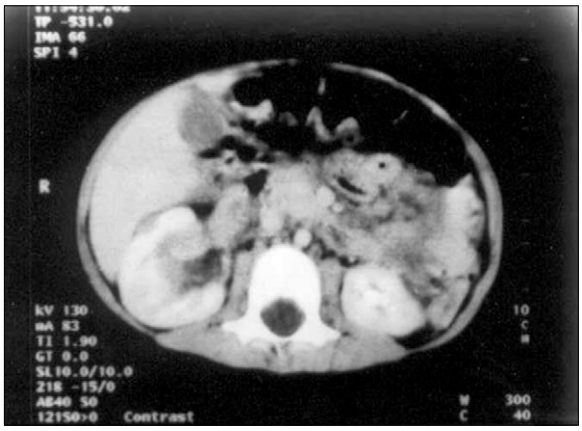

Figure 2. CT image of Wilms' tumor situated centrally in the right kidney.

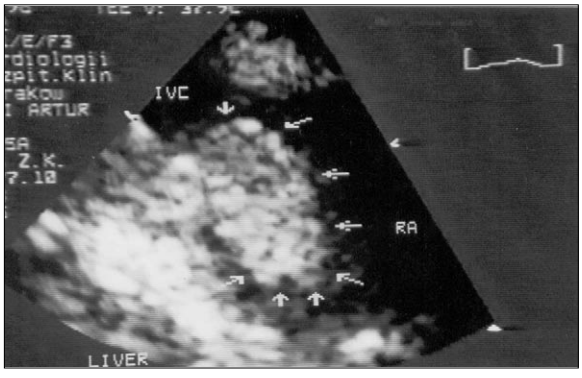

Figure 3. Transesophageal ECHO. Extension of tumor masses (arrows) via the inferior vena cava (IVC) into the right atrium (RA).

namic disturbances (Fig. 3). Two weeks later, with the patient in cardio-pulmonary by-pass, the ostium of the inferior vena cava, covered by endocardium and obstructed along a 1-cm long segment, was excised. The uneventful postoperative course allowed for continued chemotherapy (SIOP, stage III). The histopathological results showed a standard histologic subcapsular tumor 3 × 3 × 1 cm in size, situated in the upper renal pole and predominantly fibrotic, as well as a fibrotic malignant infiltration in the renal bed. No tumor cells were found in any fragment of the excised tumor thrombus. Treatment was completed 2 years ago. The patient shows no recurrent disease, the hepatic segment of the inferior vena cava limited by the hepatic vein orifice is patent, and substitute venous blood flow from the lower part of the body involves the azygos vein and the superior vena cava.

DISCUSSION

Atrial involvement by tumor masses arising from a Wilms' tumor is a rare phenomenon, reported by various sources to occur in 0.7–4% of patients [1,3,4].

In our series, this type was observed in 2% of children with of Wilms' tumor. In three patients, the renal tumors were very large. This is consistent with the observations made by other authors, who confirm that tumor extension via the renal veins, and subsequently via the inferior vena cava to the right atrium, is found predominantly in large tumors, and thus may involve both the right (more frequent) and left renal veins [4–7]. In such patients, if no hepatic vein involvement occurs, which is manifested by the Budd-Chiari syndrome, and no hemodynamic disturbances develop as a result of tricuspid valve crossing, tumor extension into the inferior vena cava may escape detection, as it is asymptomatic, and a giant tumor hinders the visualization of the venous system [3,4,8]. Such a situation was encountered in the first patient from this series. There are isolated reports of patients with a small renal tumor and massive involvement of the venous system, the latter constituting a decisive factor in the clinical presentation [9,10]. Diagnostic problems are then associated both with the atypical presentation and the severity of the patient's condition, which often requires hospitalization in an intensive care unit (Patient No. 4).

The basic symptom of Wilms' tumor is the presence of an abdominal mass, much more rarely accompanied by a history of abdominal pain. Undoubtedly, this group of patients includes children with inferior vena cava and right atrium involvement. Of the four patients in our series, all complained of abdominal pain, two were hospitalized for presumed appendicitis, and one was subjected to an appendectomy. Similar observations have been presented by Patel, although in comparison to the National Wilms' Tumor Study-3, a history of abdominal pain was noted in only 18% of patients with inferior vena cava and right atrium involvement [1,10]. Reversing the problem, the venous system should be well visualized in all children with Wilms' tumor and abdominal pain, as intracaval extension may be a cause of the abdominal complaints.

As can be inferred from studies carried out by NTWS and SIOP, preoperative chemotherapy is the method of choice in children with Wilms' tumor and inferior vena cava and right atrium involvement [5,10–13]. A decrease of tumor mass within the kidney and large vessels leads to the resolution of life-threatening symptoms, an improvement in the patient's general condition, and a decrease in the number of possible surgical complications. If chemotherapy proves to be of low clinical effectiveness or the disease progresses (as in tumors with unfavorable histology), improvement may be achieved by tumor irradiation with 1000–1500 cGy. In our series, the introduction of preoperative irradiation therapy was prompted by encephalopathy, which had developed in patient no. 2. In some children, preoperative chemotherapy results in tumor mass withdrawal into the renal vein [5]. Most likely, the thrombus persists when the venous wall is infiltrated or when the mass is 'fixed' in the atrium prior to therapy. This is illustrated by intraoperative descriptions of the thrombus closely adhering to venous walls and being covered by an endocardial layer within the atrium, as was the case in patient no. 4 from our series.

The histological analysis of surgically removed tumor thrombi, some of them after preoperative chemotherapy, showed no persistent malignant cells [5,13]. Thus the question arises whether a radical surgical procedure is warranted to excise the thrombus, when possibly a more intensive chemotherapy and radiation might be sufficient. Such a management policy was effective in the first child in our series, resulting in long-term survival, restoration of inferior vena cava patency, and a complete resolution of the abnormal mass within the right atrium, which occurred gradually over many years after the completion of treatment. It appears, however, that as long as there is no method available that would be capable of searching for the presence of persistent tumor cells within the thrombus without the need for its surgical excision, a nephrectomy involving the neoplastic kidney and the removal of the thrombus are more appropriate [9,13,14]. The fourth patient from our series was managed in such a way, which markedly improved the thoroughness of the surgical excision, since no neoplastic cells were detected within the excised thrombus, and even so venous flow occurred via the innominate vein. In view of the lack of surgical complications observed in this patient and his very good tolerance of the treatment, his qualification for particular stages of therapy was appropriate. Most likely the failure to employ more radical surgical management contributed to the deaths of two patients from this series.

The involvement of the inferior vena cava and the right atrium does not directly affect the prognosis, since it is mostly related to the histology and stage of the tumor [1]. In his report, Ritchey described a relatively low cure rate achieved in these patients, amounting to approximately 70% [13], but this is a consequence of the fact that 60% of the patients he described had stage IV dis-

ease, and 23% had tumors with unfavorable histology. While evaluating the prognosis in these children, one should take into consideration the potential for numerous complications related to hemodynamic disturbances, the complexity of surgical interventions, and the typically limited experience of the managing team, resulting from the rare incidence of these tumor types.

CONCLUSIONS

The extension of Wilms' tumor to the great vessels and the right atrium indirectly affects the final outcome. Preoperative chemotherapy in children with Wilms' tumor invading the inferior vena cava and the right atrium is the method of choice. The extent of surgery depends on the outcome of preliminary chemotherapy.

REFERENCES:

1. Ritchey M, Kelalis P, Breslow N, Offord K, Shochat S, D`Angio G: Intracaval and atrial involvement with nephroblastoma: review of National Wilms Tumor Study3. J Urol, 1998; 140: 1113-8
2. Clayman R, Sheldon C, Gonzales R: Wilms` tumor an approach to vena caval intrusion. Prog Ped Surg, 1982; 15: 285
3. Nakayama D, Delorimier A, O`Neill J, Norkool P, D`Angio G: Intracardiac extension of Wilms` tumor. A report of the National Wilms` Tumor Study. Ann Surg 1986; 204: 693
4. Martinez-Guerra G, Ruano-Agular J, Rivera-Luna R et al: Wilms` tumor with intracardiac extension. Eur J Pediatr Surg. 1992; 2: 56
5. Oberholzer H, Falkson G, De Jager L: Successful management of inferior vena cava and right atrial nephroblastoma tumor thrombus with preoperative chemotherapy. Med. Pediatr Oncol 1992; 20: 61
6. Weese D, Applebaum H, Taber P: Mapping intravascular extension of Wilms` tumor with magnetic resonance imaging. J Pediatr Surg 1991; 26: 64
7. Arens R, Frand M, Rechavi G, Wood B: Radiological cases of the month. AJDC, 1992; 146: 1091
8. Huh J, Noh C, Kim Y et al: Secondary cardiac tumor in children. Pediatr Cardiol, 1999; 20: 400
9. Matloub Y. Le Gras M, Rosenberg H et al: Massive intr-atrial Wilms` tumor: a treatment dilemma. Med. Pediatr Oncol, 1997; 28: 149
10. Patel C, Rees A, Bertolone S: Intracardiac extension of Wilms` tumor. Am J Pediatr Hematol Oncol, 1989; 11: 46
11. Ritchey M, Haase G, Shochat S: Current management of Wilms` tumor. Sem Surg Oncol, 1993; 9: 502
12. Lee A, Saing H, Leung M et al: Wilms` tumor with intracardiac extension: chemotherapy before surgery. Pediatr Hematol Oncol, 1994; 11: 535
13. Ritchey M, Kelalis P, Haase G et al: Preoperative therapy for intracaval and atrial extension of Wilms` tumor. Cancer, 1993; 71: 4104
14. Thompson W, Newman K, Seibel N et al: A strategy for resection of Wilms tumor with vena cava or atrial extension. J Pediatr Surg, 1992; 27: 912